

# Why humans die — an unsolved biological problem

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Mortality is an instrument of natural selection. Evolutionary motivated theories imply its irreversibility and life history dependence. This is inconsistent with mortality data for protected populations. Accurate analysis yields mortality law, which is specific for their evolutionary unprecedented conditions, yet universal for species as evolutionary remote as humans and flies. The law is exact, instantaneous, reversible, stepwise, and allows for a rapid (within less than two years for humans) and significant mortality decrease at any (but very old) age.

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Mortality is an instrument of natural selection. In the wild, competition for scarce resources is fierce, and only relatively few genetically fittest animals survive to their evolutionary “goal” - reproduction. Even human life expectancy at birth was around 40 - 45 years just a century ago (e.g., 38.64 years for males in 1876 Switzerland [1]). Evolutionary motivated biological theories [2] imply that during and beyond reproductive age mortality irreversibly increases and strongly depends on the life history. This disagrees with the demographic observation (see, e. g., [3]) that mortality is highly plastic; that different mortalities in Eastern and Western Germanies converged few years after their unification; that Norwegian females born in 1900 at 57 years reversed to mortality they had 36 years younger (see later). Recent experiments [4] prove that the life-prolonging effect of diet in fruit flies is independent of their past, starts immediately and is lost when the dieting stops. Thus, in agreement with theoretical predictions [5], mortality in protected populations of species as remote as humans and flies has short memory, is reversible and little depends on life history. Such dominance of nurture over nature is inconsistent with any evolutionary mechanism of mortality. But then, protected populations are indeed evolutionary unprecedented. To unravel the biologically unanticipated mechanism of their mortality, note that similar situation triggered all breakthroughs in physics via analysis of experimental data, which disregarded common wisdom and preceded rather than followed any models. Luckily, accurate forecasts of human mortality, and the resulting age structure of the population, are important for economic, taxation, insurance, etc, etc, purposes. That is why quantitative studies of mortality were started [6] long before Darwin, in 1693, by the famous astronomer Halley (the discoverer of the Halley comet) and followed in 1760 by the great mathematician Euler. To better estimate and forecast mortality, demographers developed over 15 mortality approximations [7]. Total mortality depends on a multitude of unquantified factors which describe all kinds of relevant details about the popula-

tion and its environment, from conception to the age of death: genotypes; life history; acquired components; age specific factors; even the month of death and the possibility of death being the late onset genetic disease [2, 8]. Demographic approximations prove that in a given country all these factors with remarkable accuracy reduce to few parameters only. During the last century, mortality rate in Western Europe at 0, 10 and 40 years decreased correspondingly 50, 100, and 10 times. In contrast to such mortality decrease (primarily due to improving living conditions, medical ones included), the difference between mortality rates at the same age in the same calendar year is rarely more than twofold in different countries. However, demographers do not present universal mortality approximations. They are interested in the most accurate approximation of the most important and specific mortality rate in a given country or its part. To a physicist relative proximity of such approximations in different countries suggests [9] certain universality. Mortality in a population is uncontrollably heterogeneous (e.g., 1891/1900 female infant mortality is almost twice higher in Stockholm than in the rural area [10]), and changes with time. It affects different mortality characteristics in a different way. “Additive” variables, whose values in a heterogeneous population are the averages over its different groups of the same age, are invariant to any such averaging. The less heterogeneous the population and its living conditions are, the more accurate their mortality approximations are. I conjecture that a certain fraction of mortality (denote it as “canonic”) accurately yields the law, which is the same (universal) in any population where heterogeneity of additive mortality variables is restricted to accurately quantified universal limits. Such universality is sufficient to establish its law. Any heterogeneous population consists of several “restricted heterogeneity” groups. Its mortality reduces to the universal law and fractions of the population in each of the restricted heterogeneity groups. Mortality in different countries allows one to determine the universal law parameters, and to verify its predictions.

For males and females who died in a given country in a given calendar year demographic life tables list, in particular, “period” probabilities  $q(x)$  (for survivors to  $x$ ) and  $d(x)$  (for live newborns) to die between the ages  $x$  and  $(x+1)$  [note that  $d(0) = q(0)$ ]; the probability  $l(x)$  to survive to  $x$  for live newborns; the life expectancy  $e(x)$  at  $x$ . The tables also present [1] the data and procedure which allow one to calculate  $q(x)$ ,  $d(x)$ ,  $l(x)$ ,  $e(x)$  for human cohorts, which were born in a given calendar year.

Consider a heterogeneous population, consisting of the groups with the number  $N^G(x)$  of survivors to  $x$  in a group  $G$ . The total number of survivors  $N(x)$  is the sum of  $N^G(x)$  over all  $G$ . Thus,  $l(x) = N(x)/N(0) = \sum c_G \ell^G(x) = \langle \ell^G(x) \rangle$  is the average of  $\ell^G(x)$  over all groups, with  $c_G$  and  $\ell^G(x)$  being the ratio of the population and the survivability to  $x$  in the group  $G$ . Similarly,  $d(x) = \ell(x) - \ell(x+1)$  reduces to its average over the groups of the same age. In contrast,  $q(x) = 1 - \ell(x+1)/\ell(x)$  reduces to  $q^G(y)$  in the groups of all ages  $y$  from 0 to  $x$ , since the probability  $\ell(x)$  to survive to  $x$  equals  $p(0)p(1)\dots p(x-1)$ , where  $p(y) = 1 - q(y)$  is the probability to survive from  $y$  to  $(y+1)$ . The most age specific additive variable is  $d(x)$ . (Naturally, it allows one to calculate all other mortality characteristics, e. g.,  $q(x)$ ). The most time specific one is  $d(0) = q(0)$  – it depends on the time span less than 2 years (from conception to 1 year). Thus, the most specific relation between two additive variables is the relation between  $d(x)$  and infant mortality  $q(0)$ . A universal restriction on the heterogeneity of  $q(0)$  is  $q_j < q^G(0) < q_{j+1}$ , where  $q_j$ ,  $q_{j+1}$  determine the universal for all humans boundaries of the  $j$ -th interval. Universal law implies that the relation between canonic  $d(x)$  and  $q(0)$  in any universal interval is the same as the relation between their values in any of the restricted heterogeneity groups, i.e. that  $d(x) = f_x[q(0)]$ ;  $d^G(x) = f_x[q^G(0)]$ , where  $f_x$  is a universal function. (Here and further on  $d$ ,  $q$ , etc denote canonic quantities). Since additive  $d(x) = \langle d^G(x) \rangle$ ,  $q(0) = \langle q^G(0) \rangle$ , so  $\langle f_x[q^G(0)] \rangle = f_x[\langle q^G(0) \rangle]$ . According to a simple property of stochastic variables [9], if the average of a function is equal to the function of the average, then the function is linear. So,

$$d(x) = a_j(x)q(0) + b_j(x) \quad \text{if} \quad q_j < q(0) < q_{j+1}, \quad (1)$$

where parameters  $a_j$ ,  $b_j$  for a given  $x$  are universal constants. (Here and on I skip their argument  $x$ ). When canonic infant mortality  $q(0)$  reaches an interval boundary (1), it must homogenize to the boundary value. Since  $d(x)$  at all ages reduce to infant mortality, they simultaneously reach the interval boundary and, together with  $q(0)$ , homogenize there. [Two such “ultimate” boundaries are well known:  $q(x) = 0$  when nobody dies, and  $q(x) = 1$  when nobody survives at the age  $x$ ]. At different intervals linear relations are different. Thus, the universal law implies piecewise linear  $d(x)$  vs  $q(0)$  with simultaneous at all ages intersections. Any heterogeneous

population is distributed at the universal intervals. Their occupation and Eq. (1) determine piecewise linear, but non-universal relation between  $d(x)$  and  $d(0) = q(0)$ . At a given non-universal linear segment

$$d(x) = aq(0) + b \quad (2)$$

For a given  $x$  non-universal  $a$  and  $b$  reduce to the universal law parameters and to the non-universal fractions of the population in each of its linear intervals. Heterogeneity of mortality in some groups in a given country may be sufficiently low to fit into a single universal interval. Then they yield the universal law and allow for a comprehensive study of canonic mortality. Suppose that a heterogeneous population is distributed at two, e.g., the 1-st and 2-nd, universal intervals with the concentrations  $c_1$  and  $c_2 = 1 - c_1$  correspondingly. Then  $q(0) = c_1 q_1(0) + (1 - c_1) q_2(0)$ ;  $d(x) = c_1 d_1(x) + (1 - c_1) d_2(x)$ . Thus, by Eq. (1, 2),  $q_1(0) = \alpha_1 q(0)$ ,  $q_2(0) = \alpha_2 q(0)$ , where  $c_1 = (b_2 - b)/(b_2 - b_1)$ , and  $\alpha_1 = (a - a_2)/[c_1(a_1 - a_2)]$ ;  $\alpha_2 = (a_1 - a)/[(1 - c_1)(a_1 - a_2)]$ . The crossover to the next non-universal segment occurs when, e.g.,  $q_1(0)$  reaches the intersection  $q^U(0) = (b_2 - b_1)/(a_1 - a_2)$  of the first and second universal segments. Then  $q_1(0) = q^U(0)$  implies  $d^I(x) = a_1 q^I(x) + b_1$ . (A subscript  $I$  denotes an intersection). So, this non-universal intersection belongs to the first universal linear segment or its extension. Inversely, such universality is the criterion of the population distributed at two universal segments. The set of such “extended” universal segments yields the universal law, while its non-universal intersections determine the fractions of the populations at the universal intervals. A general case (when the population is distributed at more than two universal segments) is more complicated, but also reduces to the universal law and the population fractions at the segments.

To quantitatively verify the universal law, consider the number  $D(x)$  of, e.g., Swiss female deaths at a given age  $x$  in each calendar year from 1876 to 2001[1]. At 10 years  $D(10)$  decreases (together with mortality) from 126 in 1876 to 1 in 2001. At 80 years  $D(80)$  increases (together with the life expectancy) from 231 to 951. It depends on the size of the population, e.g. in 1999 Japan at 80 years it is 13,061. Its stochastic error is  $\sim 1/D^{1/2}$ . If demographic fluctuations in mortality are consistent with this (minimal for a stochastic quantity) generic error for the same age, denote the corresponding mortality as “regular”. Otherwise, denote it as “irregular”. Remarkably, mortality is irregular only during, and few years after, major wars, epidemics, food and water contamination, etc., when its change within few years is not relatively small.

To verify and determine the universal law, I approximate regular empirical  $d(x)$  vs  $d(0)$  with the minimal number of linear segments which yields their statistical accuracy for each given age  $x$ . [Figure 1 presents the examples of  $d(80)$  vs.  $q(0)$  for Japanese and French

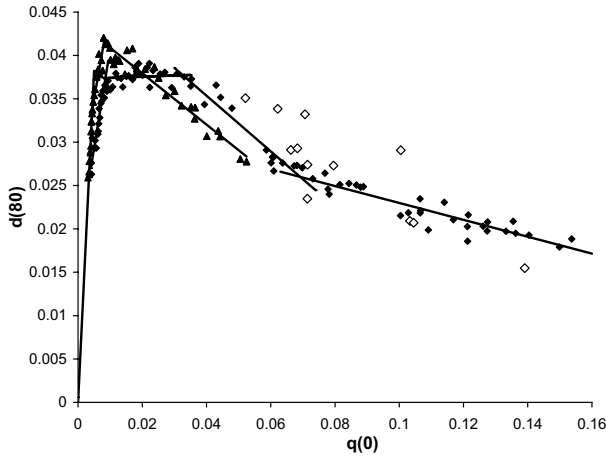


FIG. 1: The probability  $d(80)$  for newborn females in 1898-2001 France (diamonds) and 1950-1999 Japan (triangles) to die between 80 and 81 years of age vs the same calendar year infant mortality  $q(0)$ . Empty diamonds correspond to 1918 flu pandemic and World Wars. They are disregarded in the linear regressions (straight lines), which minimize the mean linear deviations from black signs to statistical 5%. When Japanese  $q(0) = 0$ , the corresponding linear regression yields  $d(80) = 0$ .

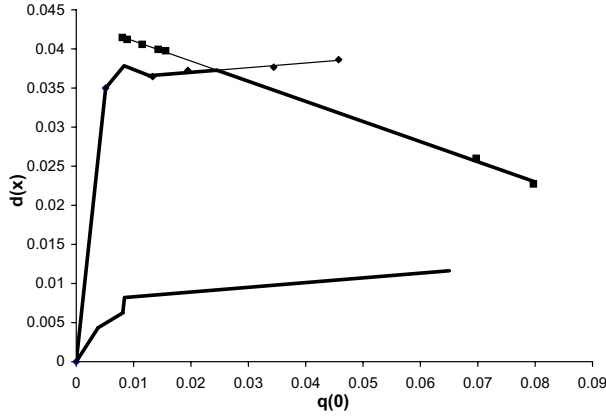


FIG. 2: Universal law of the canonic  $d(80)$  and  $d(60)$  (upper and lower curves, thick lines) vs  $q(0)$ . Note that both  $d(80) = 0$  and  $d(60) = 0$  when  $q(0) = 0$ . Diamonds and squares represent non-universal intersections for (from left to right) England (two successive intersections), France, Italy and Japan, Finland, Netherlands, Norway, Denmark, France, England correspondingly. Thin lines extend the universal linear segments.

females.] Demographic data demonstrate that all non-universal intersections in most developed countries fall on the universal straight lines (see examples in Fig. 2). Thus, the population in each such country reduces to 2 restricted heterogeneity groups (which change at the non-universal intersections). Then non-universal intersections determine the universal law (see Fig. 2). The law may be refined by accounting for a (relatively small) contribution from more than two restricted heterogeneity

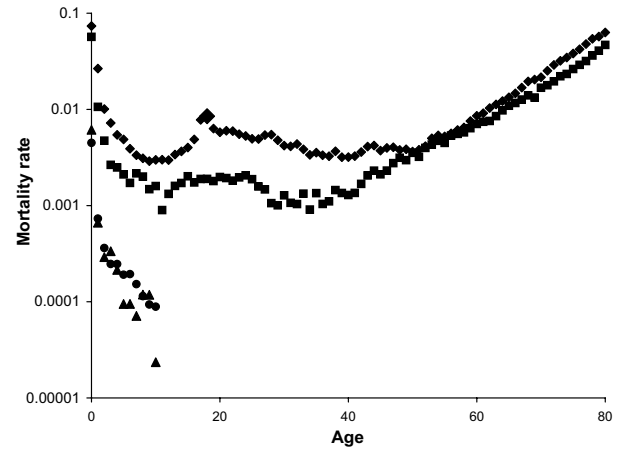


FIG. 3: Mortality rates vs age in Norwegian 1900 (diamonds, the large one for 1918 year of flu pandemic in Europe), Swedish 1920 (squares), Japanese 1989 (circles), Swiss 1990 (triangles) female cohorts.

groups.

Consider other implications and predictions of the universal law. The extrapolation of the Japanese piecewise linear dependence in Fig. 1 to  $q(0) = 0$  yields  $d(80) = 0$ , i.e. zero mortality at (and presumably prior to) 80 years. Similarly,  $d(60)$  and  $d(80)$  in Fig. 2 universally  $\rightarrow 0$  when  $q(0) \rightarrow 0$ . This is consistent with, e.g., the dependencies of the life expectancies  $e(0)$  at birth and  $e(80)$  at 80 years on the values of the same calendar year birth mortality  $q(0)$  for Japanese and French females. If nobody dies until 80, then  $e(0) = 80 + e(80)$ . In fact, the extrapolated  $e(0) = 93$  years,  $e(80) = 16$ . Thus,  $e(80) + 80 = 96$  years is just 3% higher than  $e(0)$ . Vanishing mortality may have already been observed. In 2001 Switzerland less than 17 females died in any age group from 1 till 26 years, 43 died at 40 years. In Japan, where the population is 18 times larger, 50 girls died at 10 years in 1999 (cf. Fig. 3). Such values of a stochastic quantity are consistent with zero mortality in the lowest mortality groups.

The universal law reduces the period canonic mortality at any age to the infant mortality  $q(0)$ . So, together with  $q(0)$ , at any age regular mortality rate may be rapidly reduced and reversed to its value at a much younger age. This agrees with the mortality of Norwegian and Swedish female cohorts, born in 1900 and 1920 correspondingly (Fig. 3). Both countries were neutral in the World Wars. In both infant mortality  $q(0)$  is higher than mortality  $q(80)$  at 80 years. In Sweden  $q(0)$  decreases 63-fold to  $q(11)$ , then increases 2.3-fold to  $q(24)$ . Thereafter it decreases to the same value at 34 years as 23 years earlier, at 11, and only at 45 years reaches almost the same value as 30 years younger, at 15. In Norway  $q(0)$  decreases 24.5-fold to  $q(9)$ , doubles at  $x = 21$ , halves back to the minimal value at  $x = 34$ , and then slowly changes,

until at 57 years it restores the mortality it had at 21, i.e. 36 years younger [11].

Rapid crossovers in mortality (see Fig. 1) expose several modes of the universal mechanism, which switch simultaneously for all ages (see Fig. 2). The changes amplify significant declines of old age mortality in the second half of the 20-th century [12], with its spectacular medical progress. Predicted homogenization of the mortality at the intersections was noticed for male and female mortality [5].

The non-universal law determines the non-universal population fractions in different universal intervals for a given country, sex, and calendar year. The fractions depend on genetics, life history, mutation accumulation and other factors. The difference between the total mortality and its piecewise linear approximation may be partitioned into stochastic fluctuations (which yield the Gaussian distribution), singular “irregular fluctuations” (related to, e.g., 1918 flu pandemic and world wars), and systematic deviations (related to evolutionary mechanisms [2, 5] and all unaccounted for factors). Depending on age, from 3 till 95 years the latter contribute from 2% to 10% of the total mortality. The approach may be refined if one considers several additive parameters. Preliminary study suggests this little increases the accuracy.

Regular mortality also dominates in protected populations of flies. The relations between their additive mortality variables are also piecewise linear [5]. Thus, their mortality is also predominantly universal. The (properly scaled) law, which is universal for species as remote as humans and well protected populations of flies [5] despite their different evolution, may be considered a conservation law in biology and evolution. One wonders how, why and when a law, which is specific for evolutionary unprecedented (protected) populations, could evolutionary emerge. It suggests a possibility of similar “evolutionary unmotivated” laws for other biological characteristics.

To summarize. Universal law of mortality specifies the groups whose infant mortality heterogeneity is restricted by the universal limits. In any population of any age, the law rapidly (on the scale of two years for humans) adjusts a dominant fraction of the total mortality to infant mortality and the fractions of the population in these groups. This implies that, in contrast to mortality in the wild,

mortality in well protected populations is dominated by a genetically programmed intrinsic mechanism which provides its unprecedented rapid adaptation to current living conditions. The universal form and relatively high accuracy (mostly on the scale of mortality fluctuations) of the law make it a universal and biologically explicit demographic approximation of the total mortality. The law provides certain clues to its possible physiology and physical model.

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- [1] *Human Mortality Database* (Univ. of California, Berkeley, USA, and MPI of Demographic Research, Germany, 2003), URL <http://www.mortality.org>.
- [2] B. Charlesworth, *Evolution in Age-Structured Population* (Cambridge University Press, Cambridge, 1994); C. E. Finch and T. B. Kirkwood, *Chance, Development and Aging* (Oxford University Press, Oxford, 2000).
- [3] J. W. Vaupel, J. R. Carey, and K. Christiansen, *Science* **301**, 1679 (2003).
- [4] W. Mair, P. Goymer, S. D. Pletcher, and L. Partridge, *Science* **301**, 1731 (2003).
- [5] M. Ya. Azbel', *PNAS USA* **96**, 3303 (1999); *Exp. Geront.* **37**, 859 (2002).
- [6] E. Halley, *Phil. Trans. Roy. Soc.* **17**, 596 (1693); L. Euler, *Histoire de l'Académie Royale des Sciences et Belles-Lettres* p. 144 (1760).
- [7] A. J. Coale, P. Demeny, and B. Vaughan, *Regional Model Life Tables and Stable Populations* (Academic Press, New York, 1993), 2nd ed.; R. D. Lee and L. R. Carter, *J. Am. Stat. Assoc.* **87**, 659 (1993).
- [8] G. Doblhammer and J. M. Vaupel, *PNAS USA* **98**, 2934 (2001); L. Partridge and D. Gems, *Nature* **418**, 921 (2002); *Nature Rev. Genet.* **3**, 1650175 (2002).
- [9] M. Ya. Azbel', *Phys. Rev. E* **66**, 016107 (2002).
- [10] *Statistisk Årsbok for Sverige* (SCB Statistiska Centralbyrån, Stockholm, 1993).
- [11] More robust survivors to older ages decrease the population mortality, but much less than by 30 years. Their contribution is calculated in M. Ya. Azbel', *Proc. R. Soc. London B* **263**, 1449 (1996). It is the highest till 3 and beyond 95 years of age.
- [12] J. R. Wilmoth, L. J. Deagan, H. Lundstrom, and S. Horiochi, *Science* **289**, 2366 (2000); S. Tuljapurkar, N. Li, and C. Boe, 2000. *Nature* **405**, 789 (2000).